

Clinical
Paper

Occurrence of human papillomavirus types 16 and 18 in benign prostatic hyperplasia tissues of Saudi patients

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Human papillomavirus, type 16 (HPV-16) and type 18 (HPV-18) are known to play a role in the development of neoplastic disorders of the urogenital organs. The presence of HPV-16 and HPV-18 in prostatic tissue with benign hyperplasia has been a matter of controversy. Some investigators have reported a high prevalence of HPV-16 DNA and a low prevalence of HPV-18 DNA in prostatic tissue,¹⁻³ while others have failed to demonstrate either.⁴⁻⁶ In this study, we examined prostatic tissues of 19 cases of benign prostatic hyperplasia (BPH) from Saudi patients seen at our tertiary care medical centre to investigate the occurrence of both HPV-16 and HPV-18 DNAs by using the polymerase chain reaction (PCR), followed by Southern blot hybridisation (SBH) with type-specific probes. We also obtained void urine samples from the same patients to exclude those who show HPV-16 or HPV-18 positivity by PCR in order to ensure that the HPV DNA (if any) is in the prostatic tissue, and is not due to urethral contamination. Thirteen of the 19 patient specimens were found to be negative for HPV-16 and HPV-18 in their void urine, and their prostatic tissues were processed for HPV-16 and HPV-18 DNA detection. The chief symptoms of these patients were those of bladder outflow obstruction. Some of them developed urinary retention. Their age ranges between 61 and 80 years (mean = 70.5). Standard methods were used for DNA extraction from prostatic tissue and for the subsequent PCR and SBH.

Primers designed to amplify part of the E6 ORF were used as described by McNicol and Dodd.³ The E6 gene was chosen for PCR amplification since it is preferentially conserved and is associated with cellular transformation. HPV-16 and HPV-18 DNAs cloned separately in pBR 322 plasmid (pHPVs) were kindly provided by Dr E-M de Villiers (Heidelberg, Germany) and were used as probes in SBH.

After PCR amplification, only two of the 13 BPH tissue specimens (specimens 1 and 6) gave positive signals in SBH using a radiolabelled probe specific for HPV-16 (fig. A). Both were a co-infection with HPV-18. For HPV-18, four specimens (1, 3, 4, and 6) showed positive signals in SBH using a radiolabelled probe specific for HPV-18 (fig. B), two of which were a co-infection with HPV-16 (specimens 1 and 6).

Our data indicate that in BPH from Saudi patients there is an occurrence rate of 15.4% for each of HPV-18 (2/13) and of both HPV-16 and HPV-18 in the same specimen (2/13). HPV-16 alone was not detected. McNicol and Dodd³ demonstrated a high prevalence of HPV-16 in BPH tissues (31/56, 55.4%), low occurrence of HPV-16 and HPV-18 together (3/56, 5.4%), and no HPV-18 alone was detected. Except for the 7 specimens which they obtained by suprapubic prostatectomy where 6 were positive for HPV-16 only and 1 for both HPV-16 and HPV-18, the rest of the specimens were obtained by transurethral resection without examination of HPVs in patients' urethral epithelium, which may account for the reported high prevalence of HPV-16. In an earlier study by the same investigators,² it was reported that HPV-16 was found in 14 of 15 BPH cases (93.3%). Their results are in general agreement with those of Rotola *et al.*,⁷ who found HPV-16 in 14 of 17 BPH cases (82%). On the other hand, some investigators have reported their negative findings. In a study by Ibrahim *et al.*,⁸ a total of 10 BPH samples were proven negative for HPV by PCR and *in situ* hybridisation. Serfling *et al.*,⁶ were not able to detect HPVs in a variety of prostatic conditions. Our finding that HPV-18 was detected in more samples than HPV-16 is unique. Most studies reported rare or no detection of HPV-18 alone. In the report of McNicol and Dodd,² 3 of the 15 BPH cases were positive for HPV-18 and HPV-16, while in our study we identified 4 cases out of 13 positive for HPV-18. We cannot explain the reason for the existence of more cases of HPV-

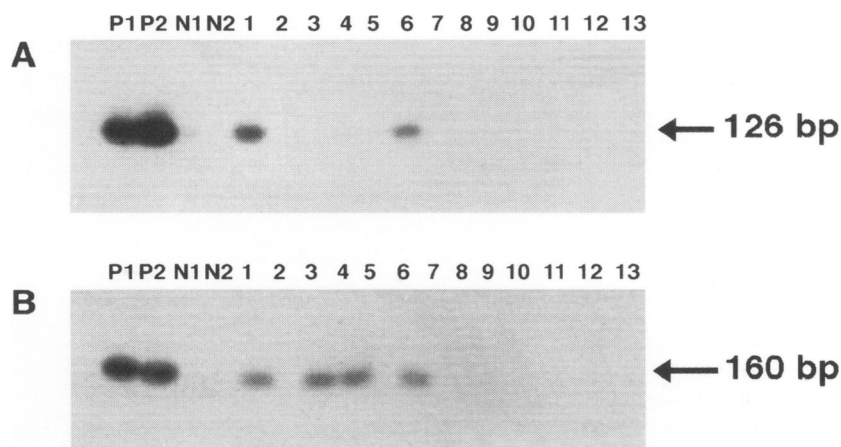
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Southern blot hybridisation profile of PCR-amplified products from the E6 sequences of HPV-16 (A) and HPV-18 (B). P1 and P2 are positive controls of plasmid-cloned HPV DNA sequences and CaSki cellular DNA for HPV-16 or HeLa cellular DNA for HPV-18, respectively. N1 and N2 are negative controls of K562 cellular DNA and reagent control, respectively. Patient samples are in lanes 1-13. The sizes of PCR products are shown by arrows on the right.

18 in our population. However, it could be due to a geographical clustering of HPV genotypes.

The conflicting results among various reports may have arisen from the use of different primers or procedures such as annealing temperatures.⁹ Primers from the E6 region of the HPV genome is able to amplify episomal and integrated HPV DNA sequences, while those from the frequently used L1 region may not amplify integrated HPV DNA.⁶ In view of the clear variation in results from many studies, more investigations should be carried out before a possible conclusion that the prostate may be a potential reservoir for the sexual transmission of high risk HPVs can be made. The use of various primers and procedures, the geographical location, and community traditions are major factors to be taken into consideration when results are interpreted.

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